American Chemistry Council | Biocides Panel

December 11, 2017

Ms. Wynne Miller
Acting Division Director
OCSPP/BEAD
United States Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Re: *Clostridium difficile* Test methods and Testing; Docket EPA-HQ-OPP-2016-0753

Dear Ms. Miller:

In March 2017, the American Chemistry Council's Biocides Panel submitted written comments on the U.S. Environmental Protection Agency's (EPA or Agency) proposed test methods and associated testing guidance for evaluating the effectiveness of antimicrobial pesticides against *Clostridium difficile* (*C. difficile*). EPA responded to the public comments in September 2017 (Response to Comments)[1] and issued its final guidance (Final Guidance),[2] but did not provide a meaningful response to several concerns raised by the Panel and other stakeholders, which we believe are consequential questions about the process EPA used to develop the *C. difficile* test method. We therefore are writing to you again, as well as bringing our concerns to the attention of EPA senior management, with a request that we meet January 11, 2018 to discuss our comments further.

While we continue our discussions on the *C. difficile* test method and guidance and until a response to this request for further clarification is provided, we ask that the Agency refrain from issuing any Data Call-Ins (DCI) to registrants of existing *C. difficile* disinfectant products with new requirements based on this method. It also is the Panel's recommendation that EPA conduct an internal review of its method development process in general as it should adopt a policy whereby any new, national test method is assessed by an independent standard setting organization such as ASTM and also vetted through a regimented, public process before it is implemented.

[1] US EPA. Agency Response to Public Comments on Draft *Clostridium difficile* Guidance Document and Methods (September 2017), Docket EPA-HQ-OPP-2016-0753.

[2] US EPA. *Methods and Guidance for Testing the Efficacy of Antimicrobial Products Against Spores of Clostridium difficile on Hard Non-Porous Surfaces* (September 2017).

## I. EPA Should Complete the Second Collaborative Study

In June 2014, EPA issued interim guidance on the testing and registration of disinfectants effective against *C. difficile* with the understanding that collaborative validation studies would be completed before new guidance was issued. The collaborative study on spore standardization was completed in 2015 and its study summary stated that "[a]n additional collaborative study is planned to fully address the performance of the efficacy procedure after the spore production and storage conditions have been verified".[3] Yet, despite its own conclusion and recognition that a second collaborative was needed, the Agency now states that an "additional collaborative investigation is not warranted at this time".[4] EPA thus issued the current guidance, suggesting regulatory change, based on statistical analysis of the first collaborative phase only.

Furthermore, the final guidance document outlines technical requirements not consistent with the collaborative testing statistical analysis. The performance criteria published was determined via statistical analysis of a collaborative study wherein three test carriers were evaluated per test lot using only one chemistry. This resulted in a need for secondary verification testing driven by the variability seen in the collaborative results. However, it should be noted that the objective of the collaborative was to standardize spore preparation, validation and storage. Given that the design of the collaborative was not to assess variability and robustness of the method, one must question the validity of the collaborative for use in setting performance criteria as a regulatory tool. In fact, this approach appears to be inconsistent with the Agency-authored guide on method validation.[5]

EPA, pursuant to the final guidance document, requires registrants to conduct testing using 10 carriers per lot while still requiring secondary verification testing. The 10 carrier replication may preclude the need for the verification testing. Without an assessment of variability across chemistries that have been tested using 10 carriers per lot, registrants may be forced to over-formulate to meet the performance criteria.

## II. EPA Should Set a Default Test Carrier

Allowing an alternative carrier for these products will help ensure that oxidizing chemistries are not disadvantaged under this method by the use of an unsuitable carrier. However, the Biocides Panel believes EPA should follow the recommendations of the scientific community and standards bodies, such as ASTM, and designate an inert material as the default carrier for all chemistries. Multiple commenters, citing to published literature, stated that artificially low efficacy results can result from the use of oxidative chemistries on non-inert steel carriers. As a consequence, the labeling and registration decisions based on these data may not be reliable and protective.

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[3] EPA-HQ-OPP-2016-0753-0004, Evaluation of Protocols for the Production and Storage of *Clostridium difficile* Spores—2015 Collaborative Study.

[4] Response to Comments, page 5.

[5] FEM Document Number 2009-01 Method Validation of U.S. Environmental Protection Agency Microbiological Methods of Analysis.

As a result, the Panel believes that the Agency should declare 304 stainless steel as the default carrier for evaluating the effectiveness of antimicrobial pesticides. 304 stainless steel was recommended by stakeholders because it is less reactive and more representative of real-world healthcare surfaces than other carriers. It also is commonly used in AOAC and European methods. In fact, 304 Stainless Steel was recently voted as the default test carrier at ASTM E35 Committee (Pesticides, Antimicrobials, and Alternative Control Agents),[6] and, thus, will be the default carrier type for the ASTM E2197 standard. It should be the default carrier for EPA as well.

## III. EPA Should Not Prematurely Adopt a Regulatory Approach

There are unintended consequences of a premature regulatory approach. We thus want to reemphasize that the use of a standard method setting organization, such as ASTM, for review, method refinements, and approval is an appropriate and necessary step prior to the implementation of a required method. The process by which guidance is being driven by a Standard Operating Procedure (SOP), ahead of method organization changes is concerning.[7] Most methodologies used by the regulated industry are governed by standard setting organizations. We believe EPA should similarly use ASTM for this proposed methodology. The method should be governed by ASTM rather than by EPA Biological and Economic Analysis Division (BEAD) lab SOP. Relying on a BEAD SOP that EPA admits will have to be aligned *in the future* with ASTM standards will result in additional and unnecessary resource burdens on both the Agency and its regulated community and will result in potentially incorrect and non-protective pesticide registration decisions.[8]

With regard to the Panel's recommendation that EPA conduct an internal review of its method development process, we would like the Agency to note that —

- In order for a method to be used as a regulatory tool, it should be scientifically suitable for its purpose (substantiation of a claim on an antimicrobial disinfectant/sanitizer label); based on real-life scenarios or predictive of real-world outcomes; scientifically defendable; and, most critically, reproducible and repeatable.[9] The involvement of standard setting organizations such as AOAC, OECD and ASTM greatly enhances the process of the development of robust and defensible standard methods that are used ultimately in the protection of public health. A standard method that has been rigorously tested and debated by the scientific community can also be useful to both the Agency and registrants during defense of products impacting public health.

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[6] ASTM E35.15 Subcommittee Meeting Minutes, New Orleans, LA (October 11-13, 2017.

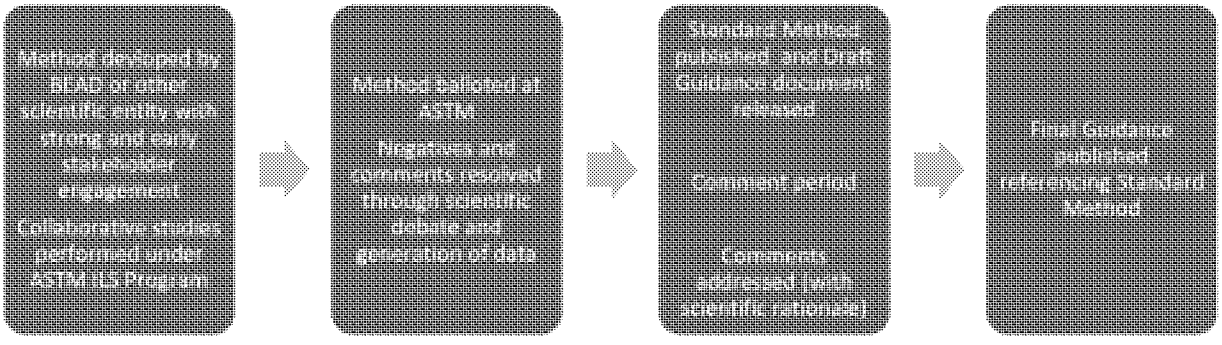
[7] *See* Response to Comments, p. 8: "EPA plans to seek comment and concurrence from experts associated with the ASTM method standardization process".

[8] *Id.*

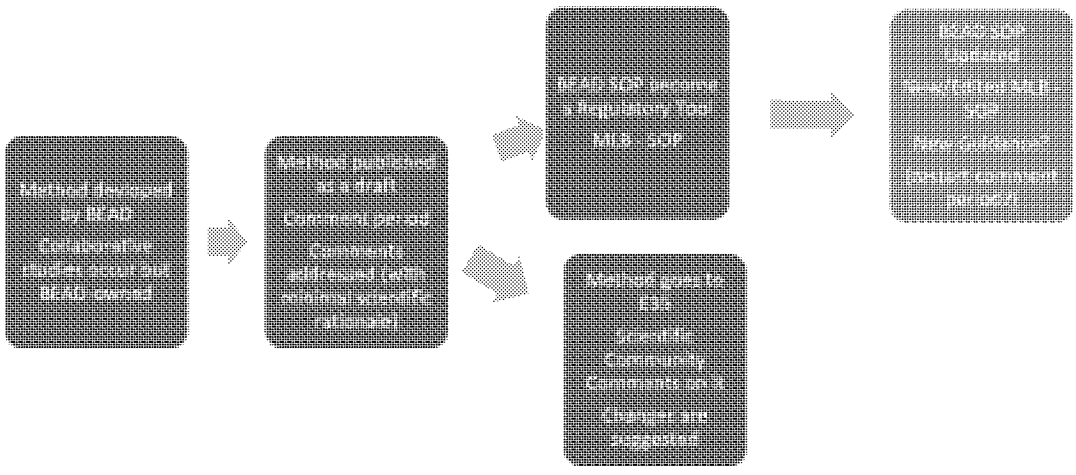
[9] *See* Tomasino, S. F (20013) Development and assessment of disinfectant efficacy test methods for regulatory purposes. American Journal of Infection Control 41 (2013) S72-S76 and FEM Document Number 2009-01 Method Validation of U.S. Environmental Protection Agency Microbiological Methods of Analysis.

- sWhile the Agency does participate in both OECD and ASTM antimicrobial committees, we ask the EPA to consider whether the involvement of these organizations is occurring at the most critical stages of EPA's method development. In the past, the Agency has successfully established agreed-upon guidelines vetted by the scientific community through one of these international standard setting organizations. Recently, however, EPA has elected to delay involvement of these organizations until after the draft/final guidance is published (e.g., the test methods for biofilm and *C. difficile*). The current practice is fraught with issues from our perspective, and, therefore, we believe it is in EPA and the registrant community's best interest that EPA have early engagement with a standard setting organization.

In order to minimize unintended consequences and to maximally leverage the collective knowledge of international regulatory and technical organizations, the Panel recommends the following process:



In comparison, the current system seems to be as follows and therefore is not as efficient and effective:



## IV. EPA Should Clarify the Implementation Timeline

Based on presentations made to the Biocides Panel by EPA's Antimicrobials Division, we understand that EPA is allowing a 12-month period, beginning from the date of the publication of the *C. difficile* method, for registrants to adopt the new method. During this time, the Agency has indicated that it will accept efficacy data that follows either the 2014 guidance or this new 2017 guidance. We support this timeline, as it is critical to allow time for proper training, SOP implementation, and other system controls when changes like these are made that may impact laboratory methodologies. As this implementation timeline is not explicitly set forth in the guidance document, we ask that EPA incorporate these dates in the document and further publish these formal implementation plans and timelines in the *Federal Register* or another widely disseminated publication for the regulated community.

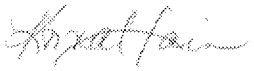
## V. Conclusion

We trust the comments above will be duly considered by the EPA and that the Agency will refrain from issuing any DCIs to registrants with new requirements based on this test method until a response to this letter is provided.

The Panel offers the Agency any assistance it requires to address our concerns and asks that we meet during the afternoon of **January 11, 2018** to discuss our comments further. Meanwhile,

please do not hesitate to contact me at 202-249-6212 or komal_jain@americanchemistry.com if you have any questions or concerns.

Sincerely,



Komal K. Jain
Executive Director, Biocides Panel
Senior Director, American Chemistry Council

Cc: Rick Keigwin, Director, OPP
Anna Lowit, Sr. Science Advisor, OPP
Steve Weiss, AD